REMARKS/ARGUMENTS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

The previous set of claims is replaced by a new set of claims. For the Examiner's information, the new claims correspond to the previous claims as follows:

New Claim(s):	Previous Claim(s):
44	9
45-48	2 and 40-42, respectively
49-50	3 and 43
51	10
52	11
53-55	12
56	27
57-58	30
59-61	31
62	32
63	33
64	34
65-68	35
69-72	36
73-74	37
75	38
76	39

Applicants respectfully submit that the new set of claims does not introduce new matter.

An early notice to that effect is earnestly solicited.

With respect to the originally claimed subject matter not claimed here, Applicants expressly reserve the right to prosecute that subject matter in a divisional application.

The sole substantive issue for consideration is the rejection of claims 1-5, 9-12 and 40-43 under 35 USC § 103(a) as being obvious over Dyrsting et al. ("Dyrsting"), US 6,077,822, in view of Rayburn, WO 00/12067, and Buschmann et al. ("Buschmann"), EP 0 693 475. In response, Applicants respectfully submit that the cited combination of references does not make out a *prima facie* case of obviousness. Moreover, the instant compounds are characterized by beneficial unexpectedly low solubility, as proven by the data in the instant specification. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

First, with respect to the scope of the claims, notwithstanding the restriction requirement, Applicants respectfully request that the Examiner examine the entire scope of new main claim 44. The entire scope of claim 44 clearly represents a proper Markush grouping characterized by (1) a common core structure, i.e., formula I; and (2) a common utility, i.e., usefulness in controlling pain. That the entire scope of claim 44 is properly examined together is, moreover, evidenced by U.S. Patent No. 6,248,737, which reissued last year as US RE39,593. An early notice that the entire scope of claim 44 is being examined is earnestly solicited.

Further, there is no compelling reason to separate the pharmaceutical composition claims from the claims to the inventive pharmaceutical salt. Both sets of claims share the same special technical feature, i.e., the inventive pharmaceutical salt, and, therefore, should be examined

together.

With respect to the method of use claims, Applicants accept rejoinder in the event the inventive pharmaceutical salt claims are allowed.

Second, Applicants respectfully submit that the cited combination of references does not make out a *prima facie* case of the obviousness of the instant claims, or lead to an expectation that the instant compounds should exhibit reduced solubility. While the Examiner relies on Rayburn as "[disclosing] that saccharinate salts of non-alkaloid bases provide improved organoleptic properties," Applicants respectfully submit that the Examine reads Rayburn much too broadly.

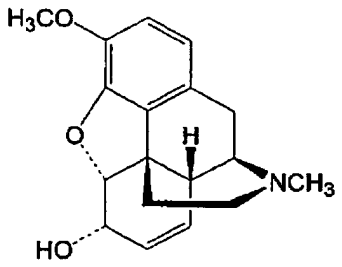
Rayburn qualifies his teachings throughout his disclosure, clearly indicating that the improvement does not apply to all non-alkaloid bases, but, rather, only to "certain" non-alkaloid bases. See, for example, page 2, lines 10-11, reading "[t]he saccharinate salt of ***certain*** non-alkaloidal organic bases provides novel salt forms demonstrating improved organoleptic properties." See, also, the next sentence on the same page, reading "[f]or ***certain*** medicinals the saccharinate salt also provides a means of sustaining drug release by virtue of decreased aqueous solubility of the saccharinate compared to more standard pharmaceutical salts such as halides, sulfates, phosphates, and the like."

Thus, Rayburn's own words expressly limit the improvement in organoleptic properties and in sustained release only to ***certain*** non-alkaloid organic bases.

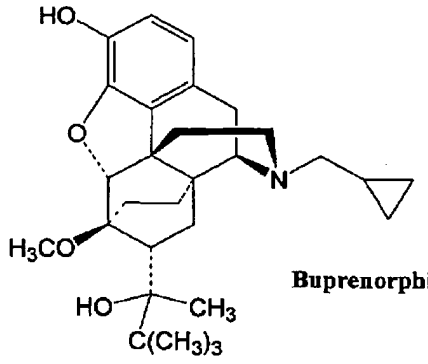
Third, beginning at page 2, line 20, Rayburn provides a list of those non-alkaloid bases to

which his invention is intended to applicable. In the case, of analgesics, Rayburn teaches the intended analgesics are those like codeine, meperidine, pentazocine, butorphanol, and buprenorphine. See, page 2, lines 25-26.

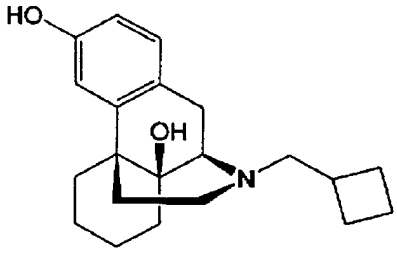
For the Examiner's convenience, Applicants reproduce the structures of these compounds hereinbelow:



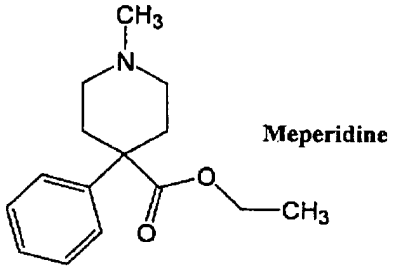
Codeine



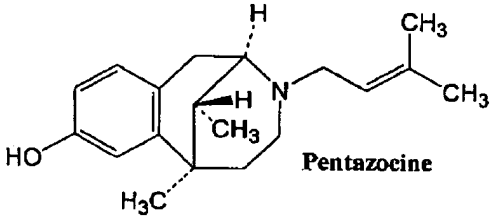
Buprenorphine



Butorphanol



Meperidine



Pentazocine

These analgesics are *structurally dissimilar* from the instant compound of formula I.

Each of these analgesics is a nitrogen-containing ***heterocyclic*** compound. And, four of the five have very complicated ***bridge*** structures. In contrast, the compound of formula I is not a nitrogen-containing heterocyclic compound, nor does it have a bridge structure at all, complicated or otherwise.

In short, a person having ordinary skill in the art would not have concluded that Rayburn's teachings were directed to compounds like those of instant formula I. Accordingly, there is nothing in the combination of Dyrsting, Rayburn and Buschmann that would have led a person having ordinary skill in the art to make a saccharinate salt of the instant compound of formula I. In the absence of a teaching or suggestion in the combination of Dyrsting, Rayburn and Buschmann that would have led a person having ordinary skill in the art to make a saccharinate salt of the instant compound of formula I, Applicants respectfully submit that such combination fails to make out a *prima facie* case of the obviousness of any of the instant claims.

Fourth, since Rayburn's teachings do not apply to the instant compound of formula I, there is also nothing in the combination of Dyrsting, Rayburn and Buschmann that would have led persons skilled in the art to expect that the saccharinate salt of the instant compound of formula I should exhibit reduced solubility compared to other common salts of the instant compound of formula I. However, the data in Table 1 in the instant specification shows quite surprisingly that the saccharinate salt of the instant compound of formula I does, in fact, exhibit beneficial reduced solubility compared to the hydrochloride and other common salts. There is absolutely nothing in the cited combination of Dyrsting, Rayburn and Buschmann that teaches or suggests this result for the instant compounds. Consequently, the data in the instant specification must be considered to be surprising and, therefore, unexpected and, thus, also as objective

evidence of nonobviousness. Although these data are not in declaration form, consistent with the rule that *all* evidence of nonobviousness must be considered when assessing patentability, the Examiner must consider data in the specification in determining whether the claimed invention provides unexpected results. *In re Soni,* 34 USPQ2d 1684, 1687 (Fed. Cir. 1995).

Fifth, Rayburn teaches that the improved organoleptic properties are beneficial, as one might expect, "in formulating oral suspensions, chewable tablets, lozenges, and quick-melt dosage forms." See, for example, page 5, lines 5-7. The saccharinate is taught to improve taste in the applicable compounds and, therefore, the improvement is advantageous where the pharmaceutical form is intended to be tasted during administration. However, the motivation to make the saccharinate due to its improved organoleptic properties is totally lacking when the pharmaceutical form is one not intended to be tasted, for example, because the pharmaceutical form is a tablet intended to be swallowed, not chewed. In other words, of what advantage it is to have an improved taste due to the saccharinate if the pharmaceutical form is to be swallowed and, thus, not tasted?

In short, Applicants see no motivation whatsoever in the cited combination of Dyrsting, Rayburn and Buschmann to make pharmaceutical forms such as are claimed in claims 58 and 61, which pharmaceutical forms would not clearly benefit from improved taste. Accordingly, Applicants respectfully request that the Examiner give special consideration to claims 58 and 61.

With respect to the requirement of claim 58 that the tablet is "not intended to be chewed," Applicants respectfully submit that such requirement does not introduce new matter. Applicants previously claimed tablets and chewable tablets and, therefore, clearly had possession of both.

Applicants are permitted to eliminate the one, i.e., chewable tablets, leaving tablets "not intended to be chewed."

In view of the foregoing, Applicants respectfully submit that the Examiner would be fully justified to reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is earnestly solicited.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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